```
=> d his

     (FILE 'HOME' ENTERED AT 17:14:42 ON 02 AUG 2004)

     FILE 'REGISTRY' ENTERED AT 17:15:03 ON 02 AUG 2004
L1                STRUCTURE UPLOADED
L2              0 S L1 SSS SAM
L3             10 S L1 SSS FULL

     FILE 'HCAPLUS, USPATFULL, CAOLD' ENTERED AT 17:16:26 ON 02 AUG 2004
L4             65 S L3
L5              0 S L4 AND (BPH OR BENIGN(3A)PROSTA?(3A)HYPERPL?)
L6           8828 S (BPH OR BENIGN(3A)PROSTA?(3A)HYPERPL?)
L7              0 S L4 AND L5
L8              0 S L4 AND L6
L9              0 S L4 AND PROSTA?(P)CARCINOM?
L10             7 S L4 AND PROSTA? AND (CARCINOM? OR CANCER? OR TUMOR?)
L11             7 DUP REM L10 (0 DUPLICATES REMOVED)

     FILE 'HCAPLUS, USPATFULL' ENTERED AT 17:23:38 ON 02 AUG 2004
L12             1 S L4 AND (TESTE? OR TESTICULAR?) AND (CANCER? OR TUMOUR? OR TUM

     FILE 'STNGUIDE' ENTERED AT 17:25:44 ON 02 AUG 2004

     FILE 'HCAPLUS, USPATFULL' ENTERED AT 17:26:32 ON 02 AUG 2004
L13             0 S L4 AND HIRSUTI?
L14             1 S L4 AND (ATRESI? OR ANOVULAT? OR DYSMENORRH? OR ACNE OR BALD?

     FILE 'STNGUIDE' ENTERED AT 17:28:46 ON 02 AUG 2004

     FILE 'HCAPLUS, USPATFULL' ENTERED AT 17:29:12 ON 02 AUG 2004
L15             2 S L4 AND ANDROGEN? AND (CARCINOM? OR CANCER? OR NEOPLAS? OR TUM
L16             2 DUP REM L15 (0 DUPLICATES REMOVED)
L17             5 S L4 AND (ANDROGEN? OR TESTOSTER? OR LUTEINIZ?)
L18             5 DUP REM L17 (0 DUPLICATES REMOVED)
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FILE 'HCAPLUS' ENTERED AT 17:29:12 ON 02 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'USPATFULL' ENTERED AT 17:29:12 ON 02 AUG 2004

=> s l4 and androgen? and (carcinom? or cancer? or neoplas? or tumor? or tumour?)
L15 2 L4 AND ANDROGEN? AND (CARCINOM? OR CANCER? OR NEOPLAS? OR TUMOR? OR TUMOUR?)

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16 2 DUP REM L15 (0 DUPLICATES REMOVED)

=> d l16 abs ibib kwic 1 2

L16 ANSWER 1 OF 2 USPATFULL on STN
AB The present invention relates to a methods of treating hot flashes and symptoms of hormonal variation in a patient, which methods include providing a tachykinin receptor antagonist and administering the tachykinin receptor antagonist to a patient experiencing a symptom of hormonal variation under conditions effective to treat the symptom of hormonal variation, which symptoms of hormonal variation can include hot flashes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:335359 USPATFULL		
TITLE:	Method of treating symptoms of hormonal variation, including hot flashes, using tachykinin receptor antagonist		
INVENTOR(S):	Guttuso, Thomas J., JR., Rochester, NY, UNITED STATES		

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003236237	A1	20031225
APPLICATION INFO.:	US 2003-609176	A1	20030627 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2001-879390, filed on 12 Jun 2001, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-211116P	20000612 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Nixon Peabody LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051
NUMBER OF CLAIMS:	21
EXEMPLARY CLAIM:	1
LINE COUNT:	562

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0004] Men may also have hot flashes following **androgen**-deprivation therapy (from bilateral orchiectomy or treatment with a gonadotrophin-releasing-hormone agonist) for metastatic prostate **cancer**.

DELACROIX

SUMM . . . effective treatment for hot flashes in women, there are women for whom such therapy is contraindicated, i.e., women with breast **cancer** or a strong family history of breast **cancer**, a history of clotting, severe migraine, or who are averse to taking the drug.

SUMM . . . tissues (e.g., total abdominal hysterectomy, bilateral salpingo-oophorectomy, etc.). In male patients, the hot flashes typically occur as a side-effect of **androgen**-dependent therapy for metastatic prostate **cancer**. They can be either surgically-induced (e.g., bilateral orchiectomy) or drug-induced (e.g., treatment with a gonadotrophin-releasing-hormone agonist, leuprolide acetate, etc.).

CLM What is claimed is:
18. The method according to claim 17, wherein the anti-**androgen** compound is leuprolide acetate.

IT 133156-06-6, GR 73632 135911-02-3, RP 67580 136982-36-0, CP 99994
138449-07-7, FK 888 142001-63-6, Saredutant 145742-28-5, CP 122721
153438-49-4, Dapitant 155418-05-6, SR 140333 157351-81-0, MEN 10627
158991-23-2, PD 154075 160492-56-8, Osanetant 168266-90-8, GR 205171
168398-02-5, GR 203040 170729-80-3, MK 869 172673-20-0, L 758298
177707-12-9, NKP 608 **204519-66-4** 214487-46-4, MEN 11467
215036-24-1, L 760735 217185-75-6, TAK 637 257888-24-7, R 116301
(tachykinin receptor antagonist for treating symptoms of hormonal variation, including hot flashes)

L16 ANSWER 2 OF 2 USPATFULL on STN

AB The present invention relates to a methods of treating hot flashes and symptoms of hormonal variation in a patient, which methods include providing a tachykinin receptor antagonist and administering the tachykinin receptor antagonist to a patient experiencing a symptom of hormonal variation under conditions effective to treat the symptom of hormonal variation, which symptoms of hormonal variation can include hot flashes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2002:27435 USPATFULL
TITLE:	Method of treating symptoms of hormonal variation, including hot flashes, using tachykinin receptor antagonist
INVENTOR(S):	Guttuso, Thomas J., JR., Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002016283	A1	20020207
APPLICATION INFO.:	US 2001-879390	A1	20010612 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-211116P	20000612 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Michael L. Goldman, NIXON PEABODY LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603
NUMBER OF CLAIMS:	31
EXEMPLARY CLAIM:	1
LINE COUNT:	590

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0004] Men may also have hot flashes following **androgen** -deprivation therapy (from bilateral orchiectomy or treatment with a gonadotrophin-releasing-hormone agonist) for metastatic prostate **cancer.**

SUMM . . . effective treatment for hot flashes in women, there are women for whom such therapy is contraindicated, i.e., women with breast **cancer** or a strong family history of breast **cancer,** a history of clotting, severe migraine, or who are averse to taking the drug.

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CLM What is claimed is:

18. The method according to claim 17, wherein the drug is an anti-**androgen** compound.

19. The method according to claim 18, wherein the anti-**androgen** compound is leuprolide acetate.

26. The method according to claim 23, wherein the patient is a male patient undergoing **androgen**-dependent therapy.

27. The method according to claim 26, wherein the **androgen** -dependent therapy is surgical or drug therapy.

IT 133156-06-6, GR 73632 135911-02-3, RP 67580 136982-36-0, CP 99994
138449-07-7, FK 888 142001-63-6, Saredutant 145742-28-5, CP 122721
153438-49-4, Dapitant 155418-05-6, SR 140333 157351-81-0, MEN 10627
158991-23-2, PD 154075 160492-56-8, Osanetant 168266-90-8, GR 205171
168398-02-5, GR 203040 170729-80-3, MK 869 172673-20-0, L 758298
177707-12-9, NKP 608 **204519-66-4** 214487-46-4, MEN 11467
215036-24-1, L 760735 217185-75-6, TAK 637 257888-24-7, R 116301
(tachykinin receptor antagonist for treating symptoms of hormonal variation, including hot flashes)

=> s l4 and (androgen? or testoster? or luteiniz?)
L17 5 L4 AND (ANDROGEN? OR TESTOSTER? OR LUTEINIZ?)

=> dup rem l17
PROCESSING COMPLETED FOR L17
L18 5 DUP REM L17 (0 DUPLICATES REMOVED)

=> d l18 abs ibib kwic 1-5

L18 ANSWER 1 OF 5 USPATFULL on STN

AB The present invention relates to a methods of treating hot flashes and symptoms of hormonal variation in a patient, which methods include providing a tachykinin receptor antagonist and administering the tachykinin receptor antagonist to a patient experiencing a symptom of hormonal variation under conditions effective to treat the symptom of hormonal variation, which symptoms of hormonal variation can include hot

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:335359 USPATFULL
TITLE:	Method of treating symptoms of hormonal variation, including hot flashes, using tachykinin receptor antagonist
INVENTOR(S):	Guttuso, Thomas J., JR., Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003236237	A1	20031225
APPLICATION INFO.:	US 2003-609176	A1	20030627 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-879390, filed on 12 Jun 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-211116P	20000612 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Nixon Peabody LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051
NUMBER OF CLAIMS:	21
EXEMPLARY CLAIM:	1
LINE COUNT:	562

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0004] Men may also have hot flashes following **androgen**-deprivation therapy (from bilateral orchiectomy or treatment with a gonadotrophin-releasing-hormone agonist) for metastatic prostate cancer.

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CLM What is claimed is:
18. The method according to claim 17, wherein the anti-**androgen** compound is leuprolide acetate.

IT 133156-06-6, GR 73632 135911-02-3, RP 67580 136982-36-0, CP 99994
138449-07-7, FK 888 142001-63-6, Saredutant 145742-28-5, CP 122721
153438-49-4, Dapitant 155418-05-6, SR 140333 157351-81-0, MEN 10627
158991-23-2, PD 154075 160492-56-8, Osanetant 168266-90-8, GR 205171
168398-02-5, GR 203040 170729-80-3, MK 869 172673-20-0, L 758298
177707-12-9, NKP 608 **204519-66-4** 214487-46-4, MEN 11467
215036-24-1, L 760735 217185-75-6, TAK 637 257888-24-7, R 116301
(tachykinin receptor antagonist for treating symptoms of hormonal variation, including hot flashes)

L18 ANSWER 2 OF 5 USPATFULL on STN

AB The present invention relates to a methods of treating hot flashes and symptoms of hormonal variation in a patient, which methods include providing a tachykinin receptor antagonist and administering the tachykinin receptor antagonist to a patient experiencing a symptom of hormonal variation under conditions effective to treat the symptom of hormonal variation, which symptoms of hormonal variation can include hot

flashes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:27435 USPATFULL
TITLE: Method of treating symptoms of hormonal variation, including hot flashes, using tachykinin receptor antagonist
INVENTOR(S): Guttuso, Thomas J., JR., Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002016283	A1	20020207
APPLICATION INFO.:	US 2001-879390	A1	20010612 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-211116P	20000612 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Michael L. Goldman, NIXON PEABODY LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
LINE COUNT: 590
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0004] Men may also have hot flashes following **androgen**-deprivation therapy (from bilateral orchiectomy or treatment with a gonadotrophin-releasing-hormone agonist) for metastatic prostate cancer.

SUMM . . . tissues (e.g., total abdominal hysterectomy, bilateral salpingo-oophorectomy, etc.). In male patients, the hot flashes typically occur as a side-effect of **androgen**-dependent therapy for metastatic prostate cancer. They can be either surgically-induced (e.g., bilateral orchiectomy) or drug-induced (e.g., treatment with a gonadotrophin-releasinghormone. . .

CLM What is claimed is:

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19. The method according to claim 18, wherein the anti-**androgen** compound is leuprolide acetate.

26. The method according to claim 23, wherein the patient is a male patient undergoing **androgen**-dependent therapy.

27. The method according to claim 26, wherein the **androgen**-dependent therapy is surgical or drug therapy.

IT 133156-06-6, GR 73632 135911-02-3, RP 67580 136982-36-0, CP 99994
138449-07-7, FK 888 142001-63-6, Saredutant 145742-28-5, CP 122721
153438-49-4, Dapitant 155418-05-6, SR 140333 157351-81-0, MEN 10627
158991-23-2, PD 154075 160492-56-8, Osanetant 168266-90-8, GR 205171
168398-02-5, GR 203040 170729-80-3, MK 869 172673-20-0, L 758298
177707-12-9, NKP 608 **204519-66-4** 214487-46-4, MEN 11467
215036-24-1, L 760735 217185-75-6, TAK 637 257888-24-7, R 116301
(tachykinin receptor antagonist for treating symptoms of hormonal variation, including hot flashes)

L18 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

AB Methods are provided for treating hot flashes and symptoms of hormonal variation in a patient, which methods include providing a tachykinin receptor antagonist and administering the tachykinin receptor antagonist to a patient experiencing a symptom of hormonal variation under conditions effective to treat the symptom of hormonal variation, which symptoms of hormonal variation can include hot flashes.

ACCESSION NUMBER: 2001:923610 HCAPLUS
DOCUMENT NUMBER: 136:31709
TITLE: Method of treating symptoms of hormonal variation, including hot flashes, using a tachykinin receptor antagonist
INVENTOR(S): Guttuso, Thomas J., Jr.
PATENT ASSIGNEE(S): University of Rochester, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095904	A1	20011220	WO 2001-US40924	20010612
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002016283	A1	20020207	US 2001-879390	20010612
EP 1299100	A1	20030409	EP 2001-942248	20010612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003236237	A1	20031225	US 2003-609176	20030627

PRIORITY APPLN. INFO.:

US 2000-211116P	P	20000612
US 2001-879390	A1	20010612
WO 2001-US40924	W	20010612

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Androgens**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(antiandrogens; tachykinin receptor antagonist for treating symptoms of hormonal variation, including hot flashes)

IT 133156-06-6, GR 73632 135911-02-3, RP 67580 136982-36-0, CP 99994
138449-07-7, FK 888 142001-63-6, Saredutant 145742-28-5, CP 122721
153438-49-4, Dapitant 155418-05-6, SR 140333 157351-81-0, MEN 10627
158991-23-2, PD 154075 160492-56-8, Osanetant 168266-90-8, GR 205171
168398-02-5, GR 203040 170729-80-3, MK 869 172673-20-0, L 758298
177707-12-9, NKP 608 **204519-66-4** 214487-46-4, MEN 11467
215036-24-1, L 760735 217185-75-6, TAK 637 257888-24-7, R 116301
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tachykinin receptor antagonist for treating symptoms of hormonal

variation, including hot flashes)

L18 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

AB The present invention is the novel use of NK-3 receptor antagonist compds. for the treatment and/or prophylaxis of diseases which are caused by high or inappropriate levels of gonadotropins and/or **androgens**, particularly **testosterone**. Antiandrogenic effects of compds. such as (S)-N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide are presented.

ACCESSION NUMBER: 2000:513508 HCAPLUS
DOCUMENT NUMBER: 133:129881
TITLE: Anti-**androgens** and methods for treating disease
INVENTOR(S): Murphy, Dennis; Wier, Patrick J.; Giardina, Giuseppe Arnaldo Maria
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043008	A1	20000727	WO 2000-US1956	20000125
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1146873	A1	20011024	EP 2000-905748	20000125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002535274	T2	20021022	JP 2000-594462	20000125

PRIORITY APPLN. INFO.:
US 1999-117059P P 19990125
WO 2000-US1956 W 20000125

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Anti-**androgens** and methods for treating disease

AB The present invention is the novel use of NK-3 receptor antagonist compds. for the treatment and/or prophylaxis of diseases which are caused by high or inappropriate levels of gonadotropins and/or **androgens**, particularly **testosterone**. Antiandrogenic effects of compds. such as (S)-N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide are presented.

ST **androgen** inhibitor; NK3 receptor antagonist; **testosterone** inhibitor

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NK3, antagonists; anti-**androgens** and for treating disease)

IT **Androgens**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiandrogens; anti-**androgens** and for treating disease)

IT Gonadotropins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; anti-**androgens** and for treating disease)

IT 160492-56-8 **174636-32-9** 224961-34-6 286367-32-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**androgens** and for treating disease)
IT 58-22-0, **Testosterone** 9002-67-9, LH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; anti-**androgens** and for treating disease)

L18 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AB Predicting blood-brain barrier (BBB) permeation remains a challenge in drug design. Since it is impossible to determine exptl. the BBB partitioning of large nos. of preclin. candidates, alternative evaluation methods based on computerized models are desirable. The present study was conducted to demonstrate the value of descriptors derived from 3D mol. fields in estimating the BBB permeation of a large set of compds. and to produce a simple math. model suitable for external prediction. The method used (VolSurf) transforms 3D fields into descriptors and correlates them to the exptl. permeation by a discriminant partial least squares procedure. The model obtained here correctly predicts more than 90% of the BBB permeation data. By quantifying the favorable and unfavorable contributions of physicochem. and structural properties, it also offers valuable insights for drug design, pharmacol. profiling, and screening. The computational procedure is fully automated and quite fast. The method thus appears as a valuable new tool in virtual screening where selection or prioritization of candidates is required from large collections of compds.

ACCESSION NUMBER: 2000:316267 HCAPLUS
DOCUMENT NUMBER: 133:114594
TITLE: Predicting blood-brain barrier permeation from three-dimensional molecular structure
AUTHOR(S): Crivori, Patrizia; Cruciani, Gabriele; Carrupt, Pierre-Alain; Testa, Bernard
CORPORATE SOURCE: Institute of Medicinal Chemistry, University of Lausanne, Lausanne-Dorigny, CH-1015, Switz.
SOURCE: Journal of Medicinal Chemistry (2000), 43(11), 2204-2216
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 50-22-6, Corticosterone 50-23-7, Cortisol 50-28-2, Estradiol, biological studies 50-47-5, Desipramine 50-49-7, Imipramine 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 51-61-6, Dopamine, biological studies 52-39-1, Aldosterone 52-86-8, Haloperidol 54-31-9 57-27-2, Morphine, biological studies 57-83-0, Progesterone, biological studies 58-00-4, Apomorphine 58-08-2, Caffeine, biological studies 58-22-0, **Testosterone** 58-39-9, Perphenazine 58-40-2, Promazine 58-73-1, Diphenhydramine 59-33-6, Mepyramine 59-92-7, Levodopa, biological studies 71-73-8 439-14-5, Diazepam 604-75-1, Oxazepam 1088-11-5, Nordazepam 4205-90-7, Clonidine 16590-41-3, Naltrexone 20290-10-2 22316-47-8, Clobazam 28797-61-7, Pirenzepine 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29122-68-7, Atenolol 29216-28-2, Mequitazine 30652-12-1, Cp21 30652-15-4, Cp24 30652-18-7, Cp25 34271-50-6 34391-04-3 34552-84-6, Isoxicam 36322-90-4, Piroxicam 51481-61-9, Cimetidine 51688-68-7 51742-87-1

53179-11-6, Loperamide 53230-10-7, Mefloquine 53772-82-0, cis-Flupentixol 53772-85-3, Trans-Flupentixol 57808-66-9, Domperidone 59429-50-4, Tamitinol 59804-37-4, Tenoxicam 66357-35-5, Ranitidine 67253-23-0 68844-77-9, Astemizole 69014-14-8, Tiotidine 69014-14-8D, Tiotidine, derivative 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 71125-38-7, Meloxicam 71351-79-6, Icotidine 74011-58-8, Enoxacine 76210-47-4 76210-49-6 79660-72-3, Fleroxacin 79794-75-5, Loratadine 79794-75-5D, Loratadine, derivs. 82419-36-1, Ofloxacin 83903-06-4, Lupitidine 85721-33-1, Ciprofloxacin 86181-42-2, Temelastine 90729-42-3, Carebastine 90729-43-4, Ebastine 92998-17-9, S-Promethazine 98079-51-7 98106-17-3, Difloxacin 98323-83-2, Carmoxirole 101363-10-4, Rufloxacin 103420-77-5, L 364718 103420-82-2 104076-38-2, Zolantidine 104076-38-2D, Zolantidine, deriv 110871-86-8, Sparfloxacin 112192-04-8, Roxindole 115900-75-9, Cp94 116003-91-9 118101-08-9 118101-09-0, L 365260 122384-14-9, L663581 123441-03-2, Rivastigmine 126055-13-8, Cp102 126588-96-3 126830-75-9 128246-10-6 130018-76-7 130018-77-8 130073-36-8 139965-10-9 139965-11-0 147368-41-0 148690-80-6 153205-46-0, EMD 61753 174635-78-0 **174636-26-1** 193222-55-8 285988-44-5 285988-45-6 285988-46-7 285988-47-8 285988-48-9 285988-49-0 285988-50-3 285988-51-4
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(blood-brain barrier permeation prediction from 3D mol. structure)

```
     (FILE 'HOME' ENTERED AT 17:14:42 ON 02 AUG 2004)

     FILE 'REGISTRY' ENTERED AT 17:15:03 ON 02 AUG 2004
L1              STRUCTURE UPLOADED
L2            0 S L1 SSS SAM
L3           10 S L1 SSS FULL

     FILE 'HCAPLUS, USPATFULL, CAOLD' ENTERED AT 17:16:26 ON 02 AUG 2004

=> s l3
L4           65 L3

=> s l4 and (BPH or benign(3a)prosta?(3a)hyperpl?)
L5            0 L4 AND (BPH OR BENIGN(3A) PROSTA?(3A) HYPERPL?)

=> s (BPH or benign(3a)prosta?(3a)hyperpl?)
L6         8828 (BPH OR BENIGN(3A) PROSTA?(3A) HYPERPL?)

=> s l4 and l5
L7            0 L4 AND L5

=> s l4 and l6
L8            0 L4 AND L6

=> s l4 and prosta?(p)carcinom?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'PROSTA?(P)CARCINOM?'
L9            0 L4 AND PROSTA?(P) CARCINOM?

=> s l4 and prosta? and (carcinom? or cancer? or tumor?)
L10           7 L4 AND PROSTA? AND (CARCINOM? OR CANCER? OR TUMOR?)

=> dup rem l10
DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L10
L11            7 DUP REM L10 (0 DUPLICATES REMOVED)

=> d l11 abs ibib kwic hitstr 1-7

L11  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2004 ACS on STN
GI
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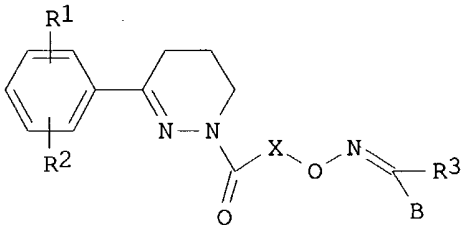

I

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AB   Title compds. [I; R1, R2 = H, OH, OR8, SR8, SOR8, SO2R8, halo; R1R2 =
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OCH2O, OCH2CH2O; R3 = H, AR7, COAR7, CO2AR7, CONH2, NH2, etc.; R7 = H, CO2H, NH2, OH, etc.; R8 = (substituted) alkyl, alkenyl, cycloalkyl, alkylenecycloalkyl, etc.; A = null, (O, S, SO, SO2, imino-interrupted) alkylene, alkenylene, cycloalkylene; B = (substituted) aryl, heteroaryl; X = (O, S, SO, SO2, imino-interrupted) alkylene], were prepared as phosphodiesterase IV inhibitors for treating osteoporosis, **tumors**, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, inflammatory processes, allergies, asthma, autoimmune diseases, myocardial diseases and AIDS (no data). Thus, 3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazine was treated sequentially with chloroacetyl chloride, N-hydroxyphthalimide, ethanolamine, and 4-methoxybenzaldehyde to give 4-methoxybenzaldehyde O-[2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl]oxime.

ACCESSION NUMBER: 2003:991488 HCAPLUS
DOCUMENT NUMBER: 140:27834
TITLE: Preparation of pyridazinyloximes as phosphodiesterase IV inhibitors.
INVENTOR(S): Eggenweiler, Hans-Michael; Beier, Norbert; Schelling, Pierre; Wolf, Michael
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003104205	A1	20031218	WO 2003-EP5173	20030516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10225574	A1	20031218	DE 2002-10225574	20020610

PRIORITY APPLN. INFO.: DE 2002-10225574 A 20020610
OTHER SOURCE(S): MARPAT 140:27834

AB . . . (substituted) aryl, heteroaryl; X = (O, S, SO, SO2, imino-interrupted) alkylene], were prepared as phosphodiesterase IV inhibitors for treating osteoporosis, **tumors**, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, inflammatory processes, allergies, asthma, autoimmune diseases, myocardial diseases and AIDS (no data).. . .

ST pyridazinyloxime prepn phosphodiesterase IV inhibitor; osteoporosis **tumor** cachexia atherosclerosis treatment pyridazinyloxime prepn; rheumatoid arthritis multiple sclerosis diabetes mellitus treatment pyridazinyloxime prepn; inflammatory process allergy asthma autoimmune disease. . .

IT AIDS (disease)

Addison's disease
Allergy
Asbestosis
Asthma
Atherosclerosis
Autoimmune disease
Cachexia
Digestive tract, disease
Drug dependence
Eczema
Emphysema
Eosinophilia
Gout
Granulation tissue
Heart, disease
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Human immunodeficiency virus 3
Infection
Inflammation
Influenza
Kidney, disease
Lupus erythematosus
Multiple sclerosis
Myasthenia gravis
Mycosis
Neoplasm
Osteoporosis
Parkinson's disease
Pneumoconiosis
Prostate gland, disease
Psoriasis
Rheumatoid arthritis
Sarcoidosis
Sepsis
Silicosis
Skin, disease
Transplant and Transplantation
Transplant rejection
Urticaria
Wilson's disease
(treatment; preparation of pyridazinyloximes as phosphodiesterase IV inhibitors)

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine maleate 124-94-7D, Triamcinolone, acetonide derivative 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoproterenol 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutalin

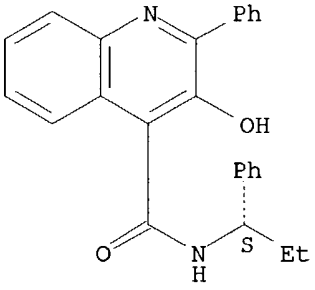
28797-61-7, Pirenzepin 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporin 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratadine 80880-90-6, Telenzepine 83799-24-0, Fexofenadine 83869-56-1, GM-CSF 83881-51-0, Cetirizine 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, Mk-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, Bay x 1005 136310-93-5, Tiotropium bromide 140841-32-3, Zd-2138 141579-54-6, Fenleuton 141579-87-5, Abbott 79175 143538-27-6, Bay x 7195 147030-01-1, Mk-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, Abbott 85761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, Sb-210661 168154-07-2, L-746530 170277-31-3, Infliximab 171964-73-1, ZD-0892 **174636-32-9**, Talnetant 185243-69-0, Etanercept 204974-93-6, BIIL 260 257892-34-5, D-4418 331731-18-1, D2E7 346735-24-8, BIIL 284 350610-64-9, NKP-608c 446023-33-2, UT-77 634206-58-9D, hydrazone derivative
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of pyridazinyloximes as phosphodiesterase IV inhibitors)

IT **174636-32-9**, Talnetant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of pyridazinyloximes as phosphodiesterase IV inhibitors)

RN 174636-32-9 HCAPLUS

CN 4-Quinolinecarboxamide, 3-hydroxy-2-phenyl-N-[(1S)-1-phenylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

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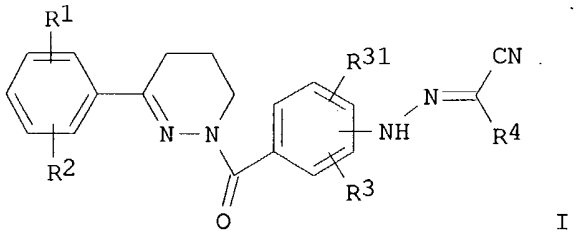


I

AB Title compds. [I; R1, R2 = H, OH, OR5, SR5, SOR5, SO2R5, X; R1R2 = OCH2O, OCH2CH2O; R3, R31 = H, R5, OH, OR5, NH2, NHR5, NHCOR5, X, CO2H, CO2R5, CONH2, etc.; R4 = cyano, tetrazolyl; R5 = (fluoro-substituted) A, cycloalkyl, (CH2)nAr; A = (fluoro- and/or chloro-substituted) alkyl, alkenyl; Ar = Ph; n = 0-2; X = F, Cl, Br, iodo], were prepared Thus, [3-(3,4-diethoxyphenyl)-5,6-dihydro-4H-pyridazine-1-yl]-(3-aminophenyl)methanone (preparation given) was stirred with NaNO2 in aqueous HCl for 1 h at -2° to 0°; malononitrile in H2O was added followed by stirring for 2 h to give a residue which was treated with KOH in MeOH to give 2-[[3-[1-[3-(3,4-diethoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]methanoyl]phenyl]hydrazono]malononitrile K salt. I were said to give a marked reduction of T cell proliferation. I are claimed for treatment of osteoporosis, **tumors**, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, inflammatory processes, allergies, asthma, autoimmune diseases, myocardial diseases, AIDS, etc.

ACCESSION NUMBER: 2003:376641 HCAPLUS
DOCUMENT NUMBER: 138:385438
TITLE: Preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as phosphodiesterase IV inhibitors.
INVENTOR(S): Eggenweiler, Hans-Michael; Wolf, Michael; Beier, Norbert; Schelling, Pierre; Ehring, Thomas
PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039548	A1	20030515	WO 2002-EP11351	20021010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2001-125455 A 20011105
OTHER SOURCE(S): MARPAT 138:385438

AB . . . salt. I were said to give a marked reduction of T cell proliferation. I are claimed for treatment of osteoporosis, **tumors**, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, inflammatory processes, allergies, asthma, autoimmune diseases, myocardial diseases, AIDS, etc.

ST pyridazinylmethanoylphenylhydrazonomalonitrile prepn phosphodiesterase inhibitor; PDE4 inhibitor hydrazonomalonitrile pyridazinylmethanoylphenyl; osteoporosis **tumor** cachexia atherosclerosis rheumatoid arthritis treatment pyridazinylmethanoylphenylhydrazonomalonitrile prepn; multiple sclerosis diabetes mellitus inflammatory process treatment pyridazinylmethanoylphenylhydrazonomalonitrile prepn; allergy asthma autoimmune disease. . .

IT Cachexia
(**cancerous**, treatment; preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as phosphodiesterase IV inhibitors)

IT **Tumor** necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulators; preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as phosphodiesterase IV inhibitors)

IT AIDS (disease)
Addison's disease
Allergy
Asbestosis
Asthma
Atherosclerosis
Autoimmune disease
Cachexia
Cystic fibrosis
Dermatomyositis
Diabetes mellitus
Digestive tract, disease
Drug dependence
Eczema
Emphysema
Eosinophilia
Fever and Hyperthermia
Gout
Granuloma
Graves' disease
Hay fever
Heart, disease
Inflammation
Influenza
Kidney, disease
Leukemia
Lupus erythematosus
Lyme disease
Multiple sclerosis
Myasthenia gravis
Mycosis
Neoplasm
Osteoarthritis
Osteoporosis
Pain
Parkinson's disease
Pneumoconiosis

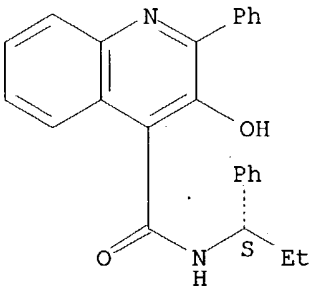
Prostate gland, disease
Psoriasis
Rheumatoid arthritis
Sarcoidosis
Sepsis
Silicosis
Skin, disease
Transplant rejection
Urticaria
Wilson's disease
(treatment; preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as phosphodiesterase IV inhibitors)

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1397-89-3, Amphotericin b 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 7440-57-5D, Gold, aurothio compds. 7683-59-2, Isoproterenol 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 22916-47-8, Miconazole 23031-25-6, Terbutaline 23593-75-1, Clotrimazole 27220-47-9, Econazole 28797-61-7, Pirenzepine 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 65277-42-1, Ketoconazole 67763-96-6, IGF-1 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratidine 80474-14-2, Fluticasone propionate 80880-90-6, Telenzepine 83799-24-0, Fexofenadine 83869-56-1, GM-CSF 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 84625-61-6, Itraconazole 86386-73-4, Fluconazole 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, Mk-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY-X 1005 128312-51-6, Ro 24-5913 136310-93-5, Tiotropium bromide 140841-32-3, Zd-2138 141579-54-6, Fenleuton 141579-87-5, Abbott 79175 143538-27-6, BAY-X 7195 147030-01-1, Mk-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, Abt-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, Sb-210661 168154-07-2, L-746530 170277-31-3, Infliximab 171964-73-1, Zd0892 **174636-32-9**, Talnetant 185243-69-0, Etanercept 202415-99-4, IPL 576092 204974-93-6, BIIL 284/260 257892-34-5, D-4418 331731-18-1, D 2E7 350610-64-9, NKP 608C 446023-33-2, UT-77
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as phosphodiesterase IV inhibitors)

IT **174636-32-9**, Talnetant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as phosphodiesterase IV inhibitors)

RN 174636-32-9 HCAPLUS
CN 4-Quinolinecarboxamide, 3-hydroxy-2-phenyl-N-[(1S)-1-phenylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AB The invention discloses the use of type 4 phosphodiesterase inhibitors (PDE IV inhibitors) to treat diseases, as well as combinations of PDE IV inhibitors with other drugs.
ACCESSION NUMBER: 2003:356269 HCAPLUS
DOCUMENT NUMBER: 138:348761
TITLE: Type 4 phosphodiesterase inhibitors and therapeutic uses thereof
INVENTOR(S): Eggenweiler, Hans-Michael; Wolf, Michael
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037349	A1	20030508	WO 2002-EP9596	20020828

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-125394 A 20011031
OTHER SOURCE(S): MARPAT 138:348761
IT **Tumor** necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TNF-α; phosphodiesterase IV inhibitors, therapeutic uses, and

use with other agents)
IT Neoplasm
(**cancerous** cachexia; phosphodiesterase IV inhibitors, therapeutic uses, and use with other agents)
IT AIDS (disease)
Addison's disease
Allergy inhibitors
Analgesics
Anemia (disease)
Anti-AIDS agents
Anti-infective agents
Anti-inflammatory agents
Anti-ischemic agents
Antiarthritics
Antiasthmatics
Antidepressants
Antidiabetic agents
Antihypertensives
Antiparkinsonian agents
Antipyretics
Antirheumatic agents
Antitumor agents
Antiviral agents
Asbestosis
Asthma
Autoimmune disease
Bronchodilators
Cachexia
Cardiovascular agents
Cognition enhancers
Cystic fibrosis
Cytomegalovirus
Dermatitis
Dermatomyositis
Digestive tract, disease
Drug dependence
Eczema
Emphysema
Eosinophil
Eosinophilia
Fever and Hyperthermia
Fungicides
Gout
Granuloma
Graves' disease
Human
Human adenovirus
Human herpesvirus
Human herpesvirus 3
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Human immunodeficiency virus 3
Infection
Influenza
Influenza virus
Ischemia
Kidney, disease

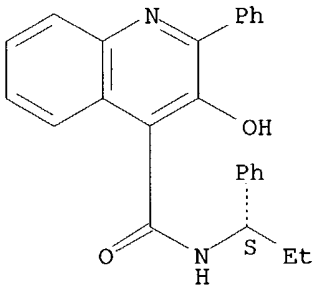
Leukemia
Lupus erythematosus
Multiple sclerosis
Myasthenia gravis
Nervous system agents
Osteoarthritis
Osteoporosis
Pain
Parkinson's disease
Pneumoconiosis
Prostate gland, disease
Psoriasis
Rheumatoid arthritis
Sarcoidosis
Sepsis
Silicosis
Urticaria
Wilson's disease
(phosphodiesterase IV inhibitors, therapeutic uses, and use with other agents)

IT 404-86-4, Capsaicin 83869-56-1, GM-CSF 171964-73-1, ZD-0892; **174636-32-9**, Talnetant 257892-34-5, D-4418 350610-64-9, NKP-608C 446023-33-2, UT-77
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cmsphosphodiesterase IV inhibitors, therapeutic uses, and use with other agents)

IT **174636-32-9**, Talnetant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cmsphosphodiesterase IV inhibitors, therapeutic uses, and use with other agents)

RN 174636-32-9 HCAPLUS
CN 4-Quinolinecarboxamide, 3-hydroxy-2-phenyl-N-[(1S)-1-phenylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AB The invention concerns the synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivs., their physiol. acceptable salts, stereoisomers, solvates, mixts. thereof and their use as phosphodiesterase VII inhibitors in the treatment

of diseases that are influenced by the phosphodiesterase VII regulation of human eosinophil activation and degranulation. Osteoporesis, **tumors**, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, AIDS, autoimmune and heart diseases can be treated with the drugs. Thus the synthesis of 5-isopropyl-4-oxo-7-p-tolyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidine-6-carboxylic acid Et ester and analog compds. is described along with injection, suppository, tablet and other formulations.

ACCESSION NUMBER: 2003:506580 HCAPLUS
DOCUMENT NUMBER: 139:79178
TITLE: Synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivatives and use as phosphodiesterase VII inhibitors and in combination with other agents
INVENTOR(S): Eggenweiler, Hans-Michael; Wolf, Michael
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: Ger. Offen., 36 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10163991	A1	20030703	DE 2001-10163991	20011224
WO 2003055882	A1	20030710	WO 2002-EP12533	20021108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2001-10163991 A 20011224
OTHER SOURCE(S): MARPAT 139:79178

AB . . . in the treatment of diseases that are influenced by the phosphodiesterase VII regulation of human eosinophil activation and degranulation. Osteoporesis, **tumors**, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, AIDS, autoimmune and heart diseases can be treated with the drugs. Thus. . .

IT Cachexia
(**cancerous**; synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivs. and use as phosphodiesterase VII inhibitors and in combination with other agents)

IT **Tumor** necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect on virus replication; synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivs. and use as phosphodiesterase VII inhibitors and in combination with other agents)

IT AIDS (disease)
Addison's disease
Adrenoceptor agonists
Allergy

Antiasthmatics
Asbestosis
Asthma
Asthma
Asthma
Atherosclerosis
Autoimmune disease
Bladder, disease
Cachexia
Cholinergic antagonists
Dandruff
Diabetes mellitus
Digestive tract, disease
Drug dependence
Emphysema
Eosinophil
Gout
Graves' disease
Heart, disease
Human
Kidney, disease
Klebsiella pneumoniae
Leukotriene antagonists
Leukotriene antagonists
Liver, disease
Lupus erythematosus
Lyme disease
Mental disorder
Multiple sclerosis
Myasthenia gravis
Mycoplasma pneumoniae
Osteoarthritis
Osteoporosis
Parkinson's disease
Parkinson's disease
Pneumoconiosis
Prostate gland, disease
Psoriasis
Rheumatoid arthritis
Rheumatoid arthritis
Sarcoidosis
Sepsis
Silicosis
Skin, disease
Streptococcus pneumoniae
Transplant rejection
Urticaria
Wilson's disease
(synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivs. and use as phosphodiesterase VII inhibitors and in combination with other agents)

IT 50-24-8, Prednisolone 53-03-2, Prednison 57-22-7, Vincristin 57-66-9, Probenecid 57-96-5, Sulfinpyrazon 58-55-9, Theophyllin, biological studies 59-42-7, Phenylephrine 76-25-5, Triamcinolone acetonide 90-82-4 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine maleate 317-34-0, Aminophyllin 404-86-4, Capsaicin 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Orciprenaline 865-21-4, Vinblastin

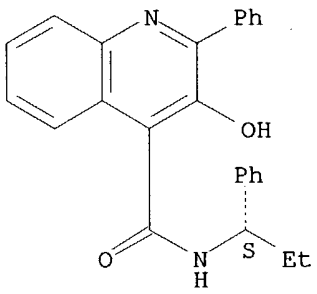
1218-35-5, Xylometazoline hydrochloride 1397-89-3, Amphotericin B 1404-26-8, Polymyxin B 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromaron 5534-09-8, Beclomethasone dipropionate 7440-57-5D, Gold, thio-compds. 7683-59-2, Isoprenalin 9004-08-4, Cathepsin 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 22916-47-8, Miconazole 23031-25-6, Terbutalin 23593-75-1, Clotrimazole 27220-47-9, Econazole 28797-61-7, Pirenzepine 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 65277-42-1, Ketoconazole 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 80880-90-6, Telenzepine 83799-24-0, Fexofenadine 83869-56-1, Granulocyte macrophage colony stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 84625-61-6, Itraconazole 86386-73-4, Fluconazole 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6, Ro 24-5913 136310-93-5, Tiotropium bromide 140841-32-3, ZD-2138 141579-54-6, Fenleuton 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, Abbott-85761 158930-07-5, L-739010 158966-92-8, Montelukast 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 171964-73-1, ZD-0892 **174636-32-9**, Talnetant 185243-69-0, Etanercept 202415-99-4, IPL 576092 204974-93-6, BIIL 284/260 257892-34-5, D-4418 350610-64-9, NKP-608C 446023-33-2, UT-77
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivs. and use as phosphodiesterase VII inhibitors and in combination with other agents)

IT **174636-32-9**, Talnetant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivs. and use as phosphodiesterase VII inhibitors and in combination with other agents)

RN 174636-32-9 HCAPLUS

CN 4-Quinolinecarboxamide, 3-hydroxy-2-phenyl-N-[(1S)-1-phenylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L11 ANSWER 5 OF 7 USPATFULL on STN

AB The present invention relates to a methods of treating hot flashes and symptoms of hormonal variation in a patient, which methods include providing a tachykinin receptor antagonist and administering the tachykinin receptor antagonist to a patient experiencing a symptom of hormonal variation under conditions effective to treat the symptom of hormonal variation, which symptoms of hormonal variation can include hot flashes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:335359 USPATFULL
TITLE:	Method of treating symptoms of hormonal variation, including hot flashes, using tachykinin receptor antagonist
INVENTOR(S):	Guttuso, Thomas J., JR., Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003236237	A1	20031225
APPLICATION INFO.:	US 2003-609176	A1	20030627 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-879390, filed on 12 Jun 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-211116P	20000612 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Nixon Peabody LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051
NUMBER OF CLAIMS:	21
EXEMPLARY CLAIM:	1
LINE COUNT:	562

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . Men may also have hot flashes following androgen-deprivation therapy (from bilateral orchiectomy or treatment with a gonadotrophin-releasing-hormone agonist) for metastatic **prostate cancer.**

SUMM . . . effective treatment for hot flashes in women, there are women for whom such therapy is contraindicated, i.e., women with breast **cancer** or a strong family history of breast **cancer,** a history of clotting, severe migraine, or who are averse to taking the drug.

SUMM . . . hysterectomy, bilateral salpingo-oophorectomy, etc.). In male patients, the hot flashes typically occur as a side-effect of androgen-dependent therapy for metastatic **prostate cancer.** They can be either surgically-induced (e.g., bilateral orchiectomy) or drug-induced (e.g., treatment with a gonadotrophin-releasing-hormone agonist, leuprolide acetate, etc.).

COMMAND INTERRUPTED
REENTER FILE 'HCAPLUS, USPATFULL, CAOLD'
AND TRY AGAIN, OR ENTER '?' FOR MORE INFORMATION.

Your command did not complete due to a temporary system problem. To recover, reenter the file you are in now. Then, any command that is normally available to you may be used. No cost summary for the

current file will be displayed. After reentering the current file you may retry your command. Also, you may wish to SAVE your search query. This can be done in any file. If you cannot access your current file, or if your command fails a second time, notify the Help Desk. Enter "HELP STN" for information on contacting the nearest STN Help Desk by telephone or by using the SEND command in STNMAIL file.

=> \

\ IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> d his

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> d his
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> file hcaplus, uspatfull

FILE 'HCAPLUS' ENTERED AT 17:23:38 ON 02 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATFULL' ENTERED AT 17:23:38 ON 02 AUG 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> s l4 and (teste? or testicular?) and (cancer? or tumour? or tumor? or carcinom? or neoplas?)
L12 1 L4 AND (TESTE? OR TESTICULAR?) AND (CANCER? OR TUMOUR? OR TUMOR? OR CARCINOM? OR NEOPLAS?)

=> d l12 abs ibib kwic 1
SUMM . . . hysterectomy, bilateral salpingo-oophorectomy, etc.). In male patients, the hot flashes typically occur as a side-effect of androgen-dependent therapy for metastatic **prostate cancer**. They can be either surgically-induced (e.g., bilateral orchiectomy) or drug-induced (e.g., treatment with a gonadotrophin-releasing-hormone agonist, leuprolide acetate, etc.).

L12 ANSWER 1 OF 1 USPATFULL on STN
AB Compounds useful as inhibitors of PDE4 in the treatment of diseases regulated by the activation and degranulation of eosinophils, especially asthma, chronic bronchitis, and chronic obstructuive pulmonary disease, of the formula: ##STR1##

wherein j is 0 or 1, provided that when j is 0, n must be 2; k is 0 or 1; m is 1, 2, or 3; n is 1 or 2; W.sup.1 and W.sup.2 are --O--; --S(.dbd.O).sub.t--, where t is 0, 1, or 2, or --N(R.sup.3)--; Y is .dbd.C(R.sup.1.sub.a)--, or --[N(O).sub.k]-- where k is 0 or 1; R.sup.1.sub.a is --H, --F, --Cl, --CN, --NO.sub.2, --(C.sub.1-C.sub.4)alkyl, --(C.sub.2-C.sub.4) alkynyl, fluorinated-(C.sub.1-C.sub.3) alkyl, fluorinated-(C.sub.1-C.sub.3) alkoxy, --OR.sup.16, or --C(.dbd.O)NR.sup.22.sub.aR.sup.22.sub.b; R.sup.A and R.sup.B are --H, --F, --CF.sub.3, --(C.sub.1-C.sub.4) alkyl, --(C.sub.3-C.sub.7) cycloalkyl, phenyl, or benzyl substituted by 0-3 R.sup.10; or R.sup.A and R.sup.B are taken together to form a spiro moiety ##STR2##

where r and s are 0-4 provided r+s is ≥1 but not >5; and X.sup.A is --CH.sub.2--, --CHF, --CF.sub.2, --NR.sup.15--, --O--, or --S(.dbd.O).sub.t--, where t is 0, 1; R.sup.C and R.sup.D are the same as R.sup.A and R.sup.B except that one of them must be --H; R.sup.1 and R.sup.2 are --H, --F, --Cl, --CN, --NO.sub.2, --(C.sub.1-C.sub.4) alkyl, --(C.sub.2-C.sub.4) alkynyl, fluorinated-(C.sub.1-C.sub.3) alkyl, --OR.sup.16), or --C(.dbd.O)NR.sup.22.sub.aR.sup.22.sub.b; R.sup.3 is --H, --(C.sub.1-C.sub.3) alkyl, phenyl, benzyl, or --OR.sup.16; R.sup.4, R.sup.5 and R.sup.6 are (a) --H, --F, --Cl, --(C.sub.2-C.sub.4) alkynyl, --R.sup.16,--OR.sup.16, --S(.dbd.O).sub.pR.sup.16, --C(.dbd.O)R.sup.16, --C(.dbd.O)OR.sup.16, --OC(.dbd.O)R.sup.16, --CN, --NO.sub.2, --C(.dbd.O)NR.sup.16R.sup.17, --OC(.dbd.O)NR.sup.16R.sup.17, --NR.sup.22.sub.aC(.dbd.O)NR.sup.16R.sup.17, --NR.sup.22.sub.aC(.dbd.NR.sup.12)NR.sup.6R.sup.17--NR.sup.22.sub.aC(.dbd.NCN)NR.sup.16R.sup.17, --NR.sup.22.sub.aC(.dbd.N--NO.sub.2)NR.sup.16R.sup.17, --C(.dbd.NR.sup.22.sub.a)NR.sup.16R.sup.17, --CH.sub.2C(.dbd.NR.sup.22.sub.a)NR.sup.16R.sup.17, --

OC(.dbd.NR.sup.22.sub.a)NR.sup.16R.sup.17, --OC(.dbd.N--NO.sub.2)NR.sup.16R.sup.17, --NR.sup.16R.sup.17, --CH.sub.2NR.sup.16R.sup.17, --NR.sup.22.sub.aC(.dbd.O)R", --NR.sup.22.sub.aC(.dbd.O)OR.sup.16, .dbd.NOR.sup.16, --NR.sup.22.sub.aS(.dbd.O).sub.pR.sup.17, --S(.dbd.O).sub.pNR.sup.16R.sup.17; or --CH.sub.2C(.dbd.NR.sup.22.sub.a)NR.sup.16R.sup.17; where p is 0, 1, or 2; (b) --(C.sub.1-C.sub.4) alkyl or --(C.sub.1-C.sub.4) alkoxy substituted by 0-3 of --F or --Cl; or 0 or 1 of (C.sub.1-C.sub.2) alkoxycarbonyl-, (C.sub.1-C.sub.2)alkylcarbonyl-, or (C.sub.1-C.sub.2) alkylcarbonyloxy-; or (c) phenyl, benzyl, furanyl, tetrahydrofuranyl, oxetanyl, thienyl, tetrahydrothienyl, pyrrolyl, pyrrolidinyl, oxazolyl, oxazolidinyl, isoxazolyl, isoxazolidinyl, thiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, pyrazolyl, pyrazolidinyl, oxadiazolyl, thiadiazolyl, imidazolyl, imidazolidinyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, piperidinyl, piperazinyl, triazolyl, triazinyl, tetrazolyl, pyranyl, azetidinyl, morpholinyl, parathiazinyl, indolyl, indolinyl, benzo[b]furanyl, 2,3-dihydrobenzofuranyl, 2-H-chromenyl, chromanyl, benzothienyl, 1-H-indazolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, or purinyl, all substituted by 0-2 of R.sup.14, or (d) R.sup.5 and R.sup.6 are taken together to form a moiety of partial Formulas (1.3.1) through (1.3.15); D is a group of partial Formulas (1.1.1) through (1.1.9): ##STR3##

where q is 1-3, provided where q is 2 or 3, R.sup.9 is --H; v is 0-1; W.sup.3 is --O--, --N(R.sup.9)--, or --OC(.dbd.O).dbd.; R.sup.7 is (a) --H; (b) --(C.sub.1-C.sub.6) alkyl, --(C.sub.2-C.sub.6) alkenyl, or --(C.sub.2-C.sub.6) alkynyl, all substituted by 0-3 of R.sup.10; (c) --(CH.sub.2).sub.u--(C.sub.3-C.sub.7) cycloalkyl where u is 0-2, substituted by 0-3 of R.sup.10; or (d) phenyl or benzyl substituted by 0-3 of R.sup.10; R.sup.8 is (a) tetrazol-5-yl, 1,2,4-triazol-3-yl, 1,2,4-triazol-3-on-5-yl, 1,2,3-triazol-5-yl, imidazol-2-yl, imidazol-4-yl, imidazolidin-2-on-4-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-on-3-yl, 1,2,4-oxadiazol-5-yl, 1,2,4-oxadiazol-3-on-5-yl, 1,3,4-oxadiazolyl, 1,3,4-oxadiazol-2-on-5-yl, oxazolyl, isoxazolyl, pyrrolyl, pyrazolyl, succinimidyl, glutarimidyl, pyrrolidonyl, 2-piperidonyl, 2-pyridonyl, 4-pyridonyl, pyridazin-3-onyl, thiadiazolyl, parathiazinyl; (b) indolyl, indolinyl, isoindolinyl, benzo[b]furanyl, 2,3-dihydrobenzofuranyl, 2-H-chromenyl, chromanyl, benzothienyl, 1H-indazolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzotriazolyl, benzotriazinyl, quinazolinyl, quinoxalinyl, pyrazolo[3,4-d]pyrimidinyl, pyrimido[4,5-d]pyrimidinyl, imidazo[1,2-a]pyridinyl, pyridopyridinyl, pteridinyl, or purinyl, all optionally substituted on a carbon atom by R.sup.14, on a nitrogen atom by R.sup.15 and all tautomer forms thereof, or on a sulfur atom by 0-2 oxygen atoms; R.sup.9 is --H, --(C.sub.1-C.sub.4) alkyl, --(C.sub.3-C.sub.7) cycloalkyl, phenyl, benzyl, --C(.dbd.O)OR.sup.16, --C(.dbd.O)R.sup.16, --OR.sup.16, --(C.sub.1-C.sub.2) alkyl-OR.sup.16, or --(C.sub.1-C.sub.2) alkyl-C(.dbd.O)OR.sup.16; or (c) --O--P(.dbd.O)(OH).sub.2 (phosphoric), --PH(.dbd.O)OH (phosphinic), --P(.dbd.O)(OH).sub.2 (phosphonic), --[P(.dbd.O)(OH)--O(C.sub.1-C.sub.4) alkyl](alkylphosphono), --P(.dbd.O)(OH)--O(C.sub.1-C.sub.4) alkyl) (alkylphosphinyl), --P(.dbd.O)(OH)NH.sub.2 (phosphoramido), --P(.dbd.O)(OH)NH(C.sub.1-C.sub.4) alkyl and --P(.dbd.O)(OH)NHR.sup.25, (substituted phosphoramido), --O--S(.dbd.O).sub.2OH (sulfuric), --S(.dbd.O).sub.2OH (sulfonic), --S(.dbd.O).sub.2NHR.sup.26 or

--NHS(.dbd.O).sub.2R.sup.26 (sulfonamido) where R.sup.26 is --CH.sub.3, --CF.sub.3, or o-toluyl, and acylsulfonamido selected from the group consisting of --C(.dbd.O)NHS(.dbd.O).sub.2R.sup.25, --C(.dbd.O)NHS(.dbd.O).sub.2NH.sub.2, --C(.dbd.O)NHS(.dbd.O).sub.2(C.sub.1-C.sub.4) alkyl, --C(.dbd.O)NHS(.dbd.O).sub.2NH(C.sub.1-C.sub.4) alkyl, --C(.dbd.O)NHS(.dbd.O).sub.2N[(C.sub.1-C.sub.4) alkyl].sub.2, --S(.dbd.O).sub.2NHC(.dbd.O)(C.sub.1-C.sub.4) alkyl, --S(.dbd.O).sub.2NHC(.dbd.O)NH.sub.2, --S(.dbd.O).sub.2NHC(.dbd.O)NH(C.sub.1-C.sub.4) alkyl, --S(.dbd.O).sub.2NHC(.dbd.O)N[(C.sub.1-C.sub.4) alkyl].sub.2, --S(.dbd.O).sub.2NHC(.dbd.O)R.sup.25, --S(.dbd.O).sub.2NHCN, --S(.dbd.O).sub.2NHC(.dbd.S)NH.sub.2, --S(.dbd.O).sub.2NHC(.dbd.S)NH(C.sub.1-C.sub.4) alkyl, --S(.dbd.O).sub.2NHC(.dbd.S)N[(C.sub.1-C.sub.4) alkyl].sub.2, or --S(.dbd.O).sub.2NHS(.dbd.O).sub.2R.sup.25, where R.sup.25 is --H, --(C.sub.1-C.sub.4) alkyl, phenyl, or --OR.sup.16; .sup.1 and .sup.2 are a moiety comprising a saturated or unsaturated carbon ring system that is 3- to 7-membered monocyclic, or that is 7- to 12-membered, fused or discontinuous, polycyclic; wherein optionally one carbon atom of said carbon ring system may be replaced by a heteroatom selected from N, O, and S; and where N is selected, optionally a second carbon atom thereof may be replaced by a heteroatom selected from N, O, and S; or a pharmaceutically acceptable salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:38198 USPATFULL			
TITLE:	Ether derivatives useful as inhibitors of PDE4 isozymes			
INVENTOR(S):	Marfat, Anthony, Mystic, CT, UNITED STATES Chambers, Robert J., Mystic, CT, UNITED STATES Magee, Thomas V., Mystic, CT, UNITED STATES			
PATENT ASSIGNEE(S):	Pfizer Inc. (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003027845	A1	20030206	
APPLICATION INFO.:	US 2002-66503	A1	20020131	(10)
	NUMBER		DATE	
PRIORITY INFORMATION:	US 2001-265304P		20010131	(60)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612			
NUMBER OF CLAIMS:	30			
EXEMPLARY CLAIM:	1			
LINE COUNT:	8073			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . and selecting inhibitors for further study. These effects include elevation of cAMP and inhibition of superoxide production, degranulation, chemotaxis, and **tumor** necrosis factor alpha (TNFα) release in eosinophils, neutrophils and monocytes. PDE4 inhibitors may induce emesis, i.e., nausea and vomiting, which,. . .

SUMM . . . pteridine class of compounds has been demonstrated to have an IC.sub.50 value of 16 nM against a PDE4 derived from **tumor** cells and to inhibit the growth of **tumor** cells at micromolar concentrations; Merz et al., "Synthesis of 7-Benzylamino-6-chloro-2-piperazino-4-pyrrolidinopteridine and novel derivatives free of

positional isomers. Potent inhibitors of cAMP-specific phosphodiesterase and of malignant **tumor** cell growth," J. Med. Chem. 41(24) 4733-4743, 1998. The pteridine PDE4 inhibitor may be represented by Formula (0.0.55): ##STR36##

SUMM . . . of renal failure; acute renal failure; cachexia; malarial cachexia; hypophysial cachexia; uremic cachexia; cardiac cachexia; cachexia suprarenalis or Addison's disease; **cancerous** cachexia; and cachexia as a consequence of infection by the human immunodeficiency virus (HIV);

SUMM . . . tryptase inhibitors; (u) platelet activating factor (PAF) antagonists; (v) monoclonal antibodies active against endogenous inflammatory entities; (w) IPL 576; (x) anti-**tumor** necrosis factor (TNFα) agents including Etanercept, Infliximab, and D2E7; (y) DMARDs including Leflunomide; (z) TCR peptides; (aa) interleukin converting enzyme. . .

SUMM . . . inhibitors on various inflammatory cell responses, which in addition to cAMP elevation, include inhibition of superoxide production, degranulation, chemotaxis and **tumor** necrosis factor (TNF) release in eosinophils, neutrophils and monocytes.

SUMM . . . skeletal muscle, prostate, and peripheral blood leukocyte (PBL) tissues. It is only weakly expressed in heart, placenta, liver, pancreas, spleen, **testes**, and ovary tissues. PDE4A and PDE4B are also strongly expressed in brain and skeletal muscle tissues, and only weakly expressed. . .

SUMM . . . induced by granulocyte-macrophage colony stimulating factor (GM-CSF) in adherent neutrophils," Clin. Exp. Immunol. 101 502-506, 1995; and Ottonello et al., "**Tumor** necrosis factor alpha-induced oxidative burst in neutrophils adherent to fibronectin: effects of cyclic AMP-elevating agents," Br. J. Haematol. 91 566-570,. . .

SUMM . . . fact that monoclonal antibodies (Mabs) to TNF-α have shown promise in R.sup.A clinical trials; Maini el al, "Beneficial effects of **tumor** necrosis factor-alpha (TNF-α blockade in rheumatoid arthritis (RA)," Clin. Exp. Immunol. 101 207-212, 1995.

SUMM . . . inhibition of rat paw edema, induced by carageenan, by oral administration of rolipram; Singh el al, "Synovial fluid levels of **tumor** necrosis factor a in the inflamed rat knee: Modulation by dexamethasone and inhibitors of matrix metalloproteinases and phosphodiesterases," Inflamm. Res.. . .

SUMM . . . eight days to twenty patients in a clinical trial has been found to effectively inhibit all of the inflammatory parameters **tested**, showing both qualitative and quantitative improvements with no adverse effects. See Hanifin et al., "Type 4 phosphodiesterase inhibitors have clinical. . .

SUMM . . . been shown to provide a protective effect. See Selmaj et al., "Prevention of chronic relapsing experimental autoimmune encephalomyelitis by soluble **tumor** necrosis factor," J. Neuroimmunol. 56 135-141, 1995. A direct correlation between the level of TNF-α mRNA and progression of EAE. . . a protective effect. See Probert et al., "Spontaneous inflammatory demyelinating disease in transgenic mice showing central nervous system-specific expression of **tumor** necrosis factor alpha," Proc. Natl. Acad. Sci. USA 92 11294-11298, 1995; and Liu et al., "TNF is a potent anti-inflammatory. . .

SUMM . . . mediators, both in vitro and in vivo. The selective PDE4 inhibitor arofylline has been shown to provide beneficial effects when **tested** in models of colitis in the rat. Further, in a dextran

sulfate induced colitis model in the rat, rolipram and. . .

SUMM [0497] Cachexia may also be the result of disease states of various types. **Cancerous** cachexia comprises the weak, emaciated condition seen in cases of malignant **tumor**. Cachexia can also be a consequence of infection by the human immunodeficiency virus (HIV), and comprises the symptoms commonly referred. . .

SUMM . . . of renal failure; acute renal failure; cachexia; malarial cachexia; hypophysial cachexia; uremic cachexia; cardiac cachexia; cachexia suprarenalis or Addison's disease; **cancerous** cachexia; and cachexia as a consequence of infection by the human immunodeficiency virus (HIV);

SUMM [0613] (v) Anti-**tumor** necrosis factor (TNFα) agents including Etanercept, Infliximab, and D2E7;

SUMM . . . wound healing agents such as peptide derivatives, yeast, panthenol, hexylresorcinol, phenol, tetracycline hydrochloride, lamin and kinetin; retinoids for treating skin **cancer**, e.g., retinol, tretinoin, isotretinoin, etretinate, acitretin, and arotinoid; mild antibacterial agents for treating skin infections, e.g., resorcinol, salicylic acid, benzoyl. . .

CLM What is claimed is:

. . . of renal failure; acute renal failure; cachexia; malarial cachexia; hypophysial cachexia; uremic cachexia; cardiac cachexia; cachexia suprarenalis or Addison's disease; **cancerous** cachexia; and cachexia as a consequence of infection by the human immunodeficiency virus (HIV); liver injury; pulmonary hypertension; and hypoxia-induced. . .

. . . Tryptase inhibitors; (v) Platelet activating factor (PAF) antagonists; (w) Monoclonal antibodies active against endogenous inflammatory entities; (x) IPL 576; (y) Anti-**tumor** necrosis factor (TNFα) agents selected from the group consisting of etanercept, infliximab, and D2E7; (z) DMARDs selected from the group. . .

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, Thiophene-2-sulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoproterenol 9004-08-4D, Cathepsin, derivs. 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 28797-61-7, Pirenzepine 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 80880-90-6, Telenzepine 83799-24-0, Fexofenadine 83869-56-1, Granulocyte-macrophage colony-stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast 100643-71-8, Desloratadine

103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor 107753-78-6, Zafirlukast 111406-87-2, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 136310-93-5, Tiotropium bromide 140841-32-3 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 171964-73-1, ZD-0892 **174636-32-9**, Talnetant 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284 350610-64-9, NKP-608C 446023-33-2, UT 77
(combination therapy with PDE4 inhibitors; preparation of carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of PDE4 isoenzymes)

=> file stnguide

FILE 'HCAPLUS' ENTERED AT 17:26:32 ON 02 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'USPATFULL' ENTERED AT 17:26:32 ON 02 AUG 2004

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L13 0 L4 AND HIRSUTI?

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L14 ANSWER 1 OF 1 USPATFULL on STN
AB The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a CNS-penetrant NK-1 receptor antagonist (e.g., a substance P receptor antagonist) in combination with an NK-3 antagonist agent. It also relates to pharmaceutical compositions containing a pharmaceutically acceptable carrier, a CNS-penetrant NK-1 receptor antagonist and an NK-3 antagonist.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:7895 USPATFULL
TITLE: Combination treatment for depression and anxiety
INVENTOR(S): Sobolov-Jaynes, Susan B., Ivoryton, CT, UNITED STATES
Lowe, John A., III, Stonington, CT, UNITED STATES
McLean, Stafford, Stonington, CT, UNITED STATES
PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004006135	A1	20040108	
APPLICATION INFO.:	US 2003-386582	A1	20030312	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-389975P	20020619 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
LINE COUNT: 6820
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . the use of tricyclic antidepressants, monoamine oxidase inhibitors, some psychotropic drugs, lithium carbonate, and electroconvulsive therapy (ECT) (see R. J. **Baldessarini** in Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th Edition, Chapter 19, McGraw-Hill, 1996 for a review). More recently,. .

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SUMM . . . partial agonists also have useful anxiolytic and other psychotropic activity, and less likelihood of sedation and dependence (see R. J. **Baldessarini** in Goodman & Gilman's Tite Pharmacological Basis of Therapeutics, 9th Edition, Chapter 18, McGraw-Hill, 1996 for a review).

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207405-30-9 207405-31-0 207405-37-6 207405-38-7 207405-42-3
(NK1 and NK3 antagonist combination treatment for depression and anxiety)